

PI Robben JPI, Van der Schueren J, Verhasselt PKM, Volckaert GLJC;  
XX WPI; 1994-062988/08.

XX Vector for positive selection of recombinants - contg. mutated  
PT selectable marker gene reactivatable by insertion of DNA to be  
PT cloned

XX Example 2; Fig 1; 27pp; Dutch.

XX A stop-codon and a unique PstI site is introduced in the cat gene  
CC of pJrtac99. The PstI site is created without alteration of  
CC the protein sequence. The mutation is obtained by exchange  
CC of a BsmI-PstI fragment with a synthetic oligonucleotide  
CC cassette. Vector pJrtac103 was obtained from transformed amber-  
CC suppressor strains. Several variants were produced: pJrtac105  
CC (one PstI site and two stop codons, pJrtac106 (one SacI site and  
CC one stop codon) and pJrtac107 (one SacI site and two stop codons).  
CC pJrtac103 was also used to create a variant having a PvuII site for  
CC the cloning of blunt fragments. The original PvuII site was deleted  
CC from the cat gene. This resulted in the replacement of Gln212 to  
CC Leu212, but did result in the loss of chloramphenicol resistance  
CC in amber-suppressor strains (pJrtac109).

XX Sequence 51 BP; 15 A; 11 C; 16 G; 9 T; 0 other;

Query Match 62.9%; Score 13.2; DB 15; Length 51;

Best Local Similarity 83.3%; Pred. No. 1.9e+03;

Matches 15; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

QY 4 ctctcatgaacagcagaag 21

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Db 7 cttaataactgcagcagaag 24

RESULT 26

AAX28029/C

ID AAX28029 standard; DNA; 30 BP.

XX AC AAX28029;

XX 10-JUN-1999 (first entry)

XX PCR primer for mammalian disabled 1 protein clone coding sequence.

XX Mammalian disabled 1 protein; mDabl; nervous system; neural development;  
KW adaptor protein; metastatic cancer; reactive gliosis; diagnosis; therapy;  
KW neurodegenerative disorder; Alzheimer's disease; screening; PCR primer;  
KW ss.

XX Synthetic.

OS Mus dunni.

XX W09909153-A1.

XX 25-FEB-1999.

XX 21-AUG-1998; 98WO-US17384.

XX 21-AUG-1997; 97US-0056473.

XX (HUTC-) HUTCHINSON CANCER RES CENT FRED.

XX Cooper JA, Howell BW;

XX WPI; 1999-181030/15.

XX New isolated mammalian Disabled protein gene - used to develop  
PT products for treating e.g. metastatic cancer, reactive gliosis,  
PT neurodegenerative diseases and Alzheimer's disease

XX Example 3; Page 30; 83pp; English.

XX

CC This sequence represents a PCR primer for DNA encoding a mammalian  
CC disabled protein 1 (mDabl) of the invention.

CC The mDabl gene is expressed as a variety of spliced mRNAs in

CC the nervous system and in some cell lines, and mDabl proteins are

CC differentially expressed and tyrosine phosphorylated during neural

CC development. When phosphorylated on tyrosine, mDabl binds to the SH2

CC domains of Src, Fyn and Abl. mDabl also forms complexes with cellular

CC phosphotyrosyl proteins through a phosphotyrosine-binding domain. mDabl

CC appears to play a role as an adaptor protein that participates in

CC development of the nervous system. It is further demonstrated that

CC disruption of the mDabl gene disturbs neuronal layering in the cerebral

CC cortex, hippocampus and cerebellum. The products can be used in screening

CC and diagnostic methods, e.g. to screen for compounds capable of

CC modulating the activity or expression of mDabl. Such compounds can be

CC used to treat e.g. metastatic cancer, reactive gliosis, neurodegenerative

CC diseases and Alzheimer's disease.

XX Sequence 30 BP; 7 A; 10 C; 6 G; 7 T; 0 other;

Query Match 61.9%; Score 13; DB 20; Length 30;

Best Local Similarity 100.0%; Pred. No. 2.2e+03;

Matches 13; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 5 ttcatgaacagca 17

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Db 30 TTCATGACAGCA 18

RESULT 27

AAT17782

ID AAT17782 standard; DNA; 38 BP.

XX AC AAT17782;

XX 11-OCT-1996 (first entry)

XX Sense primer for (Gly4Ser) VEGF.

XX Vascular endothelial growth factor; VEGF; human; conjugate; tumour; iris;  
KW proliferation inhibition; VEGF-mediated pathophysiological condition;  
KW dermatological disorder; VEGF receptor; vascular proliferation; retina;  
KW ophthalmic disorder; hyperproliferating blood vessel; therapy; psoriasis;  
KW conjunctiva; vitreous humour; rheumatoid arthritis; skin cancer; primer;  
KW varicose veins; gene therapy; polymerase chain reaction; amplify; PCR;  
KW saparin; ss.

XX Synthetic.

XX W09606641-A1.

XX 07-MAR-1996.

XX 29-AUG-1995; 95WO-US10973.

XX 16-MAY-1995; 95US-0441979.

XX 29-AUG-1994; 94US-0297961.

XX (PRIZ-) PRIZM PHARM INC.

XX Fleurbaaij GA, Freund E, Houston LL, Nova MP, Sosnowski BA;

XX Victor KD;

XX WPI; 1996-160151/16.

XX Vascular endothelial cell growth factor (VEGF) conjugates - having  
PT VEGF linked to targeted agent, used for inhibiting proliferation of  
PT cells, e.g. for gene therapy

XX Example 4; Page 87; 193pp; English.

XX This sequence represents an amplification primer for (Gly4Ser) linker

CC vascular endothelial growth factor (VEGF). The amplified sequence is  
 CC used in VEGF conjugates of the invention. In the conjugates, VEGF (or  
 CC fragments of it, see AAT17613-T17616 and AAT17739-T17750) are linked to  
 CC a targeted agent (this can be via a linker sequence), so that the  
 CC conjugate binds to a VEGF receptor. Cys-modified forms of VEGF are  
 CC particularly suitable for chemical conjugation to linkers and targeted  
 CC agents. The conjugates are used for inhibiting proliferation of cells  
 CC bearing VEGF receptors. They can be used for treating a VEGF-mediated  
 CC pathophysiological condition, including dermatological disorders with  
 CC underlying vascular proliferation, solid tumours or an ophthalmic  
 CC disorder of hyperproliferating blood vessels of the retina, iris,  
 CC conjunctiva or vitreous humour. The conjugates can also be used for  
 CC treating psoriasis, rheumatoid arthritis, skin cancers and other  
 CC tumours, or varicose veins. They are also suitable for use in gene  
 CC therapy.

XX Sequence 38 BP; 8 A; 11 C; 15 G; 4 T; 0 other;

Query Match 61.9%; Score 13; DB 17; Length 38;  
 Best Local Similarity 76.2%; Pred. No. 2.3e+03;  
 Matches 16; Conservative 0; Mismatches 5; Indels 0; Gaps 0;

Qy 1 gctcttcacgaacgcagagaag 21  
 ||||| || || |||||  
 Db 16 gctctgcaccaatggcagaag 36

# RESULT 28

AAT17783  
 ID AAT17783 standard; DNA; 53 BP.

XX AC AAT17783;

DT 11-OCT-1996 (first entry)

DE Sense primer for (Gly2Ser)2 VEGF.

XX Vascular endothelial growth factor; VEGF; human; conjugate; tumour; iris;  
 KW proliferation inhibition; VEGF-mediated pathophysiological condition;  
 KW dermatological disorder; VEGF receptor; vascular proliferation; retina;  
 KW ophthalmic disorder; hyperproliferating blood vessel; therapy; psoriasis;  
 KW conjunctiva; vitreous humour; rheumatoid arthritis; skin cancer; primer;  
 KW varicose veins; gene therapy; polymerase chain reaction; amplify; PCR;  
 KW saporin; ss.

XX Synthetic.

PN W09606641-A1.

XX 07-MAR-1996.

XX 29-AUG-1995; 95WO-US10973.

XX 16-MAY-1995; 95US-0441979.

PR 29-AUG-1994; 94US-0297961.

XX (PRIZ-) PRIZM PHARM INC.

XX PI Fleurbaaij GA, Freund E, Houston LL, Nova MP, Sosnowski BA;  
 PI Victor KD;

XX WPI; 1996-160151/16.

XX Vascular endothelial cell growth factor (VEGF) conjugates - having  
 PT VEGF linked to targeted agent, used for inhibiting proliferation of  
 PT cells, e.g. for gene therapy

XX Example 4; Page 87; 193pp; English.

XX This sequence represents an amplification primer for (Gly2Ser)2 linker  
 CC vascular endothelial growth factor (VEGF). The amplified sequence is  
 CC used in VEGF conjugates of the invention. In the conjugates, VEGF (or

CC fragments of it, see AAT17613-T17616 and AAT17739-T17750) are linked to  
 CC a targeted agent (this can be via a linker sequence), so that the  
 CC conjugate binds to a VEGF receptor. Cys-modified forms of VEGF are  
 CC particularly suitable for chemical conjugation to linkers and targeted  
 CC agents. The conjugates are used for inhibiting proliferation of cells  
 CC bearing VEGF receptors. They can be used for treating a VEGF-mediated  
 CC pathophysiological condition, including dermatological disorders with  
 CC underlying vascular proliferation, solid tumours or an ophthalmic  
 CC disorder of hyperproliferating blood vessels of the retina, iris,  
 CC conjunctiva or vitreous humour. The conjugates can also be used for  
 CC treating psoriasis, rheumatoid arthritis, skin cancers and other  
 CC tumours, or varicose veins. They are also suitable for use in gene  
 CC therapy.

XX Sequence 53 BP; 8 A; 16 C; 23 G; 6 T; 0 other;

Query Match 61.9%; Score 13; DB 17; Length 53;  
 Best Local Similarity 76.2%; Pred. No. 2.4e+03;  
 Matches 16; Conservative 0; Mismatches 5; Indels 0; Gaps 0;

Qy 1 gctcttcacgaacgcagagaag 21  
 ||||| || || |||||  
 Db 31 gctctgcaccaatggcagaag 51

# RESULT 29

AAAY2040/C  
 ID AAAY2040 standard; DNA; 53 BP.

XX AC AAAY2040;

DT 22-NOV-2000 (first entry)

DE Penicillium chrysogenum pcbC promoter PCR primer, SEQ ID NO:6.

XX pcbC promoter; Penicillium chrysogenum; Acromonium chrysogenum;  
 KW cephalosporin C synthetase; acetyltransferase; cefG; 7-ACA production;  
 KW 7-amino cephalosporanic acid; fermentation; open reading frame; ORF;  
 KW cephalosporin antibiotic; cefotaxime; cefazolin; ceftriaxone; cefuroxime;  
 KW ceftazidime; cefaclor; plasmid pICG1WA; pICG2WA; pICG3WA;  
 KW PCR primer; ss.

XX Penicillium chrysogenum.

XX W0200037671-A2.

XX 29-JUN-2000.

XX 21-DEC-1999; 99WO-EPI0292.

XX 22-DEC-1998; 98EP-0204469.

XX (STAM ) DSM NV.

XX Bovenberg RAL, Kerkman R, Koenhen E;

XX WPI; 2000-442686/38.

XX Improved in vivo production of cephalosporins, comprising fermenting  
 PT Penicillium chrysogenum transformed with a nucleic acid encoding an  
 PT expandase, a hydroxylase and an acetyltransferase -

XX Example 1; Page 16; 17pp; English.

XX The invention relates to a novel method of producing 7-amino  
 CC cephalosporanic acid (ACA), comprising fermenting a recombinant  
 CC Penicillium chrysogenum with an acyl side chain precursor, N-deacetylating  
 CC the product, and optionally acylating the free amino group or  
 CC substituting the 3' acetate group with a side chain to form a  
 CC cephalosporin antibiotic. The recombinant Penicillium chrysogenum is  
 CC capable of expressing the enzymes desacetoxycephalosporin synthetase  
 CC ("expandase"), desacetylcephalosporin C synthetase ("hydroxylase") and